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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/594,164

09/26/2006

Takashi Sugioka

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03/17/2009

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EXAMINER

CLARK, SARA E

ART UNIT

PAPER NUMBER

4121

MAIL DATE

DELIVERY MODE

03/17/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/594,164	Applicant(s) SUGIOKA ET AL.	
	Examiner SARA E. CLARK	Art Unit 4121	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-18 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____. |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>12/20/2006</u> . | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

This is a national stage (35 U.S.C. 371) application of PCT/JP05/06828, filed 3/31/2005, which claims benefit of priority to Japanese application 2004-108419, filed 3/31/2004. Claims 1-18, as amended, are pending.

Priority

1. Acknowledgment is made of applicant's claim to foreign priority under 35 U.S.C. 119(a)-(d). A proper claim was made on the ADS filed 9/26/2006 and the certified copy of Japanese application 2004-108419 has been received. Thus, claims 1-18 are entitled to an effective filing date of 3/31/2005, and a priority date of 3/31/2004.

Information Disclosure Statement

2. The information disclosure statement (IDS) submitted on 12/20/2006 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Specification

3. The disclosure is objected to because of the following informalities: the side chain hydroxyl group is identified throughout as the 21-hydroxyl group, although structural formulae I-IV show the hydroxyl group bonded to carbon 22 (see Moss, IUPAC Nomenclature of Steroids, p. 3). To avoid confusion, this Office Action refers to the side chain hydroxyl group as the 21-hydroxyl group, consistent with the specification and claims. However, appropriate correction is required.

Claim Objections

4. Claims 1-18 are objected to because of the following informalities: the side chain hydroxyl group is identified as the 21-hydroxyl group, although structural formulae I-IV show the hydroxyl group bonded to carbon 22 (see Moss, IUPAC Nomenclature of Steroids, p. 3). To avoid confusion, this Office Action refers to the side chain hydroxyl group as the 21-hydroxyl group, consistent with the specification and claims. However, appropriate correction is required.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 1-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nakazawa et al. (US PG Pub. 2003/0180742, published 9/25/2003, supplied by Applicant on the IDS dated 12/20/2006) in view of Moriarty et al. (Tetrahed. Let. 35 (44) 8103-6, 1994).

Nakazawa et al. teach a method of producing 5 α -pregnane derivatives as intermediates useful in squalamine synthesis, starting with (20S)-7 α ,21-dihydroxy-20-methyl-pregna-1,4-dien-3-one as a reactant (Ref. Ex. 1, paras. 101-102, "the diene")

and resulting in (20S)-7 α ,21-dihydroxy-20-methyl-5 α -pregna-3-one as a product (Ex. 1, paras. 104-105, "the ketone").

Formula I-1 of Nakazawa et al. ((20S)-7 α ,21-dihydroxy-20-methyl-5 α -pregna-1,4-dien-3-one, the unprotected diene, para. 20) is identical to formula I as recited in claims 1-24, where R2 is a hydrogen atom; it is noted that Nakazawa et al. do not teach a protecting group on the C21 hydroxyl (R1 of formula I).

Formula II-1 of Nakazawa et al. ((20S)-7 α ,21-dihydroxy-20-methyl-5 α -pregna-3-one, the unprotected ketone, para. 21) is identical to formula IV as recited in claims 8-12 and 14-18; and identical to formula II where R11 and R12 are each independently a hydrogen atom, as recited in claims 1-7 and 13.

Formula III-1 of Nakazawa et al. ((20S)-7 α ,21-di-(O-protecting group)-20-methyl-5 α -pregna-3-one, the protected ketone, para. 22) is identical to formula III as recited in claims 8-12 and 14-18, where R21 and R22 are each a hydroxyl-protecting group.

The method of Nakazawa et al. teaches the steps of

(a) reducing the diene with lithium in the presence of ammonia (known as the Birch reduction) to reduce the double bonds at C1-C2 and C4-C5 to single bonds (paras. 12, 13, 50), in the presence of a proton donor such as ethanol (paras. 53, 72), as recited in claims 1-18; and

(b) protecting the C7 and C21 hydroxyl groups of the ketone with tert-butyl-dimethylsilyl protecting groups (paras. 14, 15, 42), as recited in claims 1-18.

While Nakazawa et al. teach all the steps, reactants, products, and reagents of the claimed invention, the reference does not teach compound I where the C21 hydroxyl

group of the diene is protected and the 7α -hydroxyl is not, as recited in claims 2 and 9.

Nakazawa et al. also do not teach the reduction and protection steps in the reverse order as recited in the claims, i.e., protecting the hydroxyl group(s) prior to the reduction step.

Moriarty et al. does teach hydroxyl-group protection prior to the reduction step as part of a multi-step synthesis of squalamine, in which the similarly reactive side chain hydroxyl group at C24 is protected with a tert-butyldimethylsilyl protecting group (step iv, yielding compound 4, pp. 8103-4), before the ene-one compound is subjected to the Birch reduction, using lithium in ammonia and ethanol (step vi, yielding compound 6 in 81% yield, p. 8104). Due to the reactivity of sterol side chain hydroxyl groups as compared to, for example, hydroxyl groups at C3 or C7, a result of steric effects, inductive effects, and other factors, the C24 hydroxyl protecting group of Moriarty et al. remains in place for most of the synthesis (twelve steps) before deprotection (step v, yielding compound 16, pp. 8104-5), recited as step (b) in claims 8-12 and 14-18. Further, Moriarty et al. teach the 7α -hydroxy group as unprotected for most of the synthesis following its introduction (nine steps) before a protecting group is added after deprotection of the C21 hydroxyl group. Thus, Moriarty et al. teach what Nakazawa does not, i.e., protecting the side chain hydroxyl group prior to the reduction step, while leaving the 7α -hydroxy group unprotected.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to synthesize (20S)- 7α ,21-dihydroxy-20-methyl- 5α -pregna-3-one using the same method and reagents taught by Nakazawa et al. but

with the two steps reversed as taught by Moriarty et al., because, as recognized by MPEP 2144.04, selection of any order of performing process steps is *prima facie* obvious in the absence of new or unexpected results (*In re Burhans*, 154 F.2d 690, 69 USPQ 330 (CCPA 1946)).

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to

be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 1-3 and 13 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 2 of copending Application No. 10/594,163. Although the conflicting claims are not identical, they are not patentably distinct from each other because

- where R3 and R4 in combination form a bond, formula I recited in examined claims 1-3 and 13 is identical to formula I in reference claim 2, to include the scope of variable groups R1 and R2;
- formula II recited in examined claims 1-3 and 13 is identical to formula II in reference claim 2, to include the scope of variable groups R11 and R12;
- the process recited in examined claims 1-3 and 13 is identical to the process recited in reference claim 2, to include the production of a mixture of formulae II and III recited in reference claim 2, because
- while examined claims 1-3 and 13 do not explicitly read on formula III recited in reference claim 2, they do so implicitly, since reference formula III is necessarily formed as part of the process of examined claims 1-3 and 13, so that a mixture of compounds of reference formulae II and III is inherently produced by the process of examined claims 1-3 and 13.

In other words, examined claims 1-3 and 13 recite a reactant, a process, and product (a mixture of formula II and reference formula III which is formed as the reaction proceeds to completion) identical to the reactant, process, and product of reference claim 2.

9. Claims 4, 5, 14, and 15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 4 of copending Application No. 10/594,164. Although the conflicting claims are not identical, they are not patentably distinct from each other (a) for the reasons given in paragraph 8 above, and (b) in addition, the hydroxyl protecting species recited in reference claim 4 anticipates the genus recited in examined claims 4 and 14, and is identical to the species recited in examined claims 5 and 15.

10. Claims 6 and 7 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 6 of copending Application No. 10/594,164. Although the conflicting claims are not identical, they are not patentably distinct from each other (a) for the reasons given in paragraph 8 above, and (b) in addition, the metal species recited in reference claim 6 anticipates the genus recited in examined claim 6, and is identical to the species recited in examined claim 7.

11. Claims 8-10 and 16 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 8 of copending Application No. 10/594,164. Although the conflicting claims are not identical, they are not patentably distinct from each other because

- where R3 and R4 in combination form a bond, formula I recited in examined claims 8-10 and 16 is identical to formula I in reference claim 8, to include the scope of variable groups R1 and R2;
- formula III recited in examined claims 8-10 and 16 is identical to formula IV in reference claim 8, to include the scope of variable groups R21 and R22;
- formula IV recited in examined claims 8-10 and 16 is identical to formula VI in reference claim 8;
- the two-step process recited in examined claims 8-10 and 16 is identical to the process recited in reference claim 8, to include the production of a mixture of formulae IV and V, then a mixture of VI and VII recited in reference claim 8, because
- while examined claims 8-10 and 16 do not explicitly read on formulae V and VII recited in reference claim 8, they do so implicitly, since reference formulae V and VII are necessarily formed as part of the process of examined claims 8-10 and 16, so that a mixture of compounds of reference formulae IV and V, then VI and VII, is inherently produced by the process of examined claims 8-10 and 16.

In other words, examined claims 8-10 and 16 recite a reactant, a process, and product (instant formula IV) identical to the reactant, process, and product (reference formulae VI) of reference claim 8.

12. Claims 11, 12, 17, and 18 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 10 of copending Application No. 10/594,164. Although the conflicting claims are not

identical, they are not patentably distinct from each other (a) for the reasons given in paragraph 11 above, and (b) in addition, the hydroxyl protecting species recited in reference claim 10 anticipates the genus recited in examined claims 11 and 17, and is identical to the species recited in examined claims 12 and 18.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

13. Claims 1-18 are rejected.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SARA E. CLARK whose telephone number is (571) 270-7672. The examiner can normally be reached on Mon - Thu, 7:30 am - 5:00 pm (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patrick J. Nolan can be reached on 571-272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

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USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SEC

/Patrick J. Nolan/

Supervisory Patent Examiner, Art Unit 4121